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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/868,953	09/19/2001	Kazuo Suzuki	3190-010	9938

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EXAMINER
KEMMERER, ELIZABETH

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 12/03/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/868,953	SUZUKI ET AL.	
	Examiner	Art Unit	
	Elizabeth C. Kemmerer, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6 & 8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of Application, Amendment, And/Or Claims

The preliminary amendments filed 19 September 2001 (Paper No. 7) and 04 November 2002 (Paper No. 11) have been entered in full. The sequence listing is free of errors and has been entered into the file.

Claims 1-10 are under examination.

Specification

It is noted that the specification is replete with grammatical and syntax errors due to its being a translation from a foreign document. Although no requirement is made, Applicant is invited to correct such errors, including errors in technical terminology, as it is in the interest of the public to have a patent written as clearly as possible. Of course, new matter must be avoided.

35 U.S.C. § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-4 and 8-10 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. It is not clear if the claimed "bone resorption inhibitor" is a compound (such as a protein) or a composition comprising a protein. A broad, reasonable interpretation of the claims indicates that the former interpretation is

encompassed by the claims. Such proteins can be found in nature. Products of nature do not constitute patentable subject matter.

This rejection can be amended in one of at least two ways. First, the claims can be amended to recite that the bone resorption inhibitor is "isolated" or "purified". Second, the claims can be amended to clarify that the recited bone resorption inhibitor is a composition: "a bone resorption inhibitor **composition** comprising..."

35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is not clear whether claims 1-4 and 8-10 are directed to bone resorption inhibitor compounds or compositions, as discussed above. Thus, the metes and bounds of the claimed invention cannot be determined.

Additionally, claim 2 recites amino acid positions without any reference sequence. In the absence of a reference sequence, it cannot be determined which sequence is intended.

Claim 5 does not clearly recite a method step. It merely recites a determination step, which is a mental process. For example, it is not clear whether a **sample** is being collected and assayed for bone resorption inhibitory activity.

In claim 6, there is recitation of introducing a factor or substances, but there is no recitation of what the factor or substances are added to.

In claim 7, there is no recitation that the substances or factor are present in an amount effective to achieve inhibition of bone resorption. Thus, the method step does not clearly relate back o the goal set forth in the preamble.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed invention wherein the recited leukocyte activating protein factor comprises SEQ ID NO: 1, does not reasonably provide enablement for other proteins or substances derived from SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1-4 and 8-10 are directed either to compounds or compositions (see discussion above) comprising a leukocyte activating protein factor or leukocyte activating protein factor-derived substances of undefined structure which have the activity of inhibiting bone resorption. Claim 5 is directed to a method of screening for such a factor or substance; claim 6 is directed to a method of producing bone resorption

inhibitors; and claim 7 is directed to a method of inhibiting bone resorption in an animal comprising administering the factor or substances to the animal. The specification discloses a protein comprising SEQ ID NO: 1 which is shown to have bone resorption inhibitory activity by the pit formation assay. The scope of patent protection sought by Applicant as defined by the claims does not bear a reasonable correlation with the scope of enabling disclosure set forth in the specification for the following reasons.

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can

be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone (Bork, 2000, Genome Research 10:398-400; Skolnick et al., 2000, Trends in Biotech. 18(1):34-39, especially p. 36 at Box 2; Doerks et al., 1998, Trends in Genetics 14:248-250; Smith et al., 1997, Nature Biotechnology 15:1222-1223; Brenner, 1999, Trends in Genetics 15:132-133; Bork et al., 1996, Trends in Genetics 12:425-427). Furthermore, the scope of the structure of the factors or substances recited in the claims is broader than only proteins. Mimetics (including organic compounds, inorganic compounds, or small molecules) are also encompassed by the term "substances". Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation

on protein structure and function, and the breadth of the claims which fail to recite any structural limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claims 1-10 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims recite leukocyte activating protein factor-derived substances without any structural limitations.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

With the exception of SEQ ID NO: 1, the skilled artisan cannot envision the detailed chemical structure of the encompassed substances, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at

1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO: 1, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 and 6-10 are rejected under 35 U.S.C. 102(b) as being anticipated by EP 0 723 016 A2 (published 1996).

EP 0 723 016 A2 discloses a LECT2 polypeptide of SEQ ID NO: 6 which is identical to the instant LECT2 polypeptide of SEQ ID NO: 1. Although EP 0 723 016 A2

does not disclose that their LECT2 protein has bone resorption inhibitory activity, such activity is inherent to the protein recited in claims 1-4 and 8-10.

If claims 1-4 and 8-10 are interpreted to be directed to a compound, EP 0 723 016 A2 teaches this compound.

If claims 1-4 and 8-10 are directed to a bone resorption inhibitor composition comprising the compound, then the phrase "bone resorption inhibitor" is interpreted as an intended use and is given no patentable weight in this art rejection. The composition comprising LECT2 disclosed by EP 0 723 016 A2 is consistent with use in therapy, and has overlapping effective doses absent evidence to the contrary.

Regarding claim 6, EP 0 723 016 A2 discloses a method of producing a composition comprising their disclosed protein, thus meeting the limitations of the claim as interpreted without giving the intended use term "bone resorption inhibitor" any patentable weight as discussed above.

Regarding claim 7, the phrase "for bone resorption inhibiting" is interpreted as intended use and is not given patentable weight. EP 0 723 016 A2 discloses administration of their protein to an animal, thus meeting the limitations of the step recited in the claim.

Allowable Subject Matter

The instant application enables bone resorption inhibitor compositions comprising the polypeptide of SEQ ID NO: 1 and methods of administering same to achieve bone resorption inhibition. The prior art does not recognize that the protein of

SEQ ID NO: 1 has bone resorption inhibitory activity. Therefore, methods of administering the polypeptide of SEQ ID NO: 1 to an animal in an amount effective to achieve inhibition of bone resorption would be allowable. Compositions comprising the polypeptide of SEQ ID NO: 1 and other compounds known to be effective for inhibiting bone resorption would also be free of the art, since the art would not suggest combining the protein of SEQ ID NO: 1 with such compounds. However, it is not clear that the instant specification has support for such compositions.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth C. Kemmerer, Ph.D. whose telephone number is (703) 308-2673. The examiner can normally be reached on Mon. - Thurs., 6:30 to 4:00, and alternate Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne L. Eyler, Ph.D. can be reached on (703) 308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Elizabeth C. Kemmerer

ECK
December 2, 2002